Resuscitating clinical research in the United Kingdom

John Bell on behalf of the working group of Academy of Medical Sciences

Clinical research in Britain is in decline. A new report from the Academy of Medical Sciences sets out the action urgently needed to revitalise it

Our knowledge of the basic mechanisms of disease has increased greatly over the past 20 years. A substantial gulf remains, however, between basic discoveries and converting such discoveries into innovations that can be applied to patients. This translational barrier can be bridged only through clinical research. Concerned at the state of clinical research in the United Kingdom, the Academy of Medical Sciences established a working group to identify the problems and suggest solutions.

State of UK research

The working group's report focuses on serious weakness in two key areas: experimental medicine and clinical trials (box). Up until the 1970s, the United Kingdom was internationally recognised for its contribution to characterising diseases by careful examination and testing in patients. However, the development of methods to investigate the molecular and genetic basis of disease has since shifted research away from the bedside and into the laboratory. The surge in activity in molecular science has led to a substantial reduction in both research and researchers in clinical science. Pressure on NHS beds and facilities in teaching hospitals is also pushing out clinical research so that the NHS now has limited capacity to evaluate the new tools that are emerging from academia and industry.

Many of the methods used for large clinical trials, cohort studies, and meta-analyses were also developed in the United Kingdom. Application of these methods has had a big effect on the health of individuals and the NHS—for example, in showing the link between smoking and lung cancer and the benefit of statins in patients at risk of cardiovascular disease or stroke.[1 2] Despite the clear benefits of such research, funding of trials is falling from all sources.[3] Companies have expressed concerns over the last decade about the United Kingdom's decline as an attractive location for clinical trials, specifying fragmented research trial capacity, long start-up times, low patient recruitment rates, high and variable costs, regulatory constraints, and a less welcoming culture than other countries.

Importance of strong research capability

The failure of the United Kingdom to maintain these two areas of research activity is having serious consequences for its clinical research base. The lack of capacity for research will stop the translation of discoveries in basic science into clinical practice. The NHS, however, is highly dependent on critical evaluation of new diagnostic and therapeutic interventions, as the government acknowledged when it set up the National Institute for Clinical Excellence. Because health care is free at the point of access and organised according to nationally agreed standards, patients' access to new interventions needs to be based on independent data showing efficacy.

Increased research will bring other benefits. The creation of a culture within NHS facilities that values and rewards careful and thoughtful evaluation of a

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The focus on basic molecular sciences has reduced clinical research

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Members of the working group are available on bmj.com

Examples of types of study in experimental medicine and clinical trials

Experimental medicine
- Proof of concept studies
- Phase I and II (early) studies
- Evaluation of new methods of diagnosis
- Characterisation of intermediate phenotypes of surrogate markers of disease
- Assessment of new technologies

Clinical trials and population based science
- Disease networks
- Phase III trials
- Monitoring drugs and disease
- Genomic epidemiology
- Health services research

range of practices will inevitably raise the standard of clinical practice. Patients participating in clinical trials will benefit from this culture of inquiry and the rigorous protocols that are put in place. In addition, a good clinical research infrastructure allows patients in the NHS to have relatively early access to novel therapeutic interventions and clinicians to become rapidly familiar with their benefits.

Overcoming the problems

The academy's study identified several factors that limit the ability to undertake experimental research and clinical trials in the United Kingdom (box). Below, we set out the recommendations for overcoming these obstacles. Although funding is an important concern, efficient organisation of research is needed to make best use of resources.

Establish a new funding structure

An important aid to coordination would be to establish a national network for clinical research within the NHS to create and support clinical trial and translational networks. A successful framework has already been established for cancer with the National Translational Cancer Network and National Cancer Research Network. These networks coordinate the implementation of large clinical trials between centres—for example, providing support for the collection of tissue samples and recruiting patients.

The framework should be extended to include six other major disease areas: neurodegenerative disease, musculoskeletal disease, cardiovascular disease and stroke, respiratory disease, mental health, and diabetes. The resulting national network for clinical research could ensure that resources were appropriately targeted at the necessary infrastructure and would fund specific research commissions by the NHS. It would need the status of a special health authority to ensure that it had the authority to implement its programme.

Factors limiting UK research
- Lack of appropriate facilities and infrastructure
- Lack of appropriately trained clinical scientists and a career structure to support them
- Inadequate funding
- Failure to use opportunity provided by NHS to generate high quality clinical data for such studies
- Increasingly complex legal and ethical governance

Increase NHS support

The NHS should attempt to spend 1.5% of its turnover on clinical research activities. This target was set as part of the NHS research and development programme when it was conceived in 1994 but has not been achieved. The figure is reasonable considering the importance of research for cost effective health care and compares favourably with research and development budgets in the commercial sector, which are 1-16%.

Identify NHS clinical research facilities

Clinical research facilities need to be set up within or adjacent to NHS facilities to support experimental medicine. Although only a few of these facilities are realistically sustainable, they should be identified and supported through appropriately costed overhead streams accompanying grants from the major funding bodies, including the Medical Research Council, charities, the NHS, and the biotechnology and pharmaceutical industry.

Develop research in primary care

Research in primary care needs to be further developed to facilitate large scale trials, cohort studies, and patient monitoring. Any expansion must be founded on a clear definition of the research priorities of primary care trusts and be integrated with the priorities of other funders at a national level. The institution of compatible data management systems that allow records to be linked within the whole of primary care should be given priority.

Consider a national ethical code for informed consent

Large datasets produce much more robust information on outcomes from clinical trials and population based health studies. The opportunities being created by the NHS Information Strategy could potentially provide very substantial advances in this field. However, this is inhibited significantly by the constraints placed on the use of data for health research.[4] A national code for informed consent relating to use of data on patients could remove these barriers. It would allow patient records to be used for large scale cohort studies of disease and therapeutic monitoring studies (phase IV studies) in which patients themselves would be unaffected.

Encourage networking within Europe

Coordination of clinical trials throughout Europe could greatly enhance the potential of new investment in this area and would avoid duplication of effort. Existing and emerging programmes could exert pressure on regulatory authorities and help ensure that the European Clinical Trials Directive does not place unrealistic constraints on research activity.

Establish a coherent career and reward structure

Recruiting and retaining research staff is currently difficult. More support is needed for researchers at all stages of their training and long term support should be available so that clinical research scientists can

undertake their research activities and continue to participate in routine patient care within the NHS.

Existing measures of success and recognition for those working in other areas of science are often inappropriate for clinical research. Data emerging from clinical studies is seldom published in the high impact journals *Nature, Cell,* and *Science,* and the time required to move through the development and implementation of a single set of protocols is such that productivity can easily be perceived to be low. Recognition must be found for individuals undertaking clinical investigation that acknowledges the challenges associated with developing and instituting protocols in patients.

New funding should be made available

The biggest limitation to expansion of clinical research once an appropriate infrastructure is in place would be programme funding. Extra funds should be available through the Medical Research Council to support clinical trials and provide for a funding stream for experimental medicine and training clinical scientists. This money should be ring fenced. Support is also required to develop new methods for studying chronic disease, where randomised controlled trials are often inappropriate.

In response to this increase, major charities need to commit to properly resource the aspect of clinical research relevant to their interests. Attempts should also be made to ensure that the biotechnology industry and pharmaceutical companies recognise this opportunity and increase their investment in UK research. Collaboration between funders, although difficult to achieve, will be essential to fund studies that are likely to become bigger and more complex as standards of care improve.

Educate the public about merits of clinical research

Expansion of clinical research will be successful only if the public recognises its value and is willing to participate. Serious attempts must be made to ensure that people understand the benefits of clinical research, not just for those participating in studies but also for future patients who will benefit from the insights gained. In exchange, the NHS should make it possible for any patient who wishes to participate in a clinical study to have the opportunity to do so.

Conclusion

The United Kingdom is not alone in facing a decline in research. Many other countries are experiencing similar problems. However, the NHS is perhaps more dependent on a healthy research environment than other healthcare systems. Any attempt to energise clinical research will require the joint efforts of the Department of Health, the Department of Trade and Industry, the Medical Research Council, and the major medical charities. The success or failure of their efforts will have serious implications for the effective management of the NHS, for patients who require new treatments for their disease, and for those attempting to develop new medicines in the biotechnology and pharmaceutical industries.

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Competing interests: JB has been employed by the NHS and MRC for many years, both of whom could benefit from this report. He was a member of MRC Council until July 2002. He has modest equity positions in a pharmaceutical investment fund and has shares in Roche AG. He is a non-executive member of Oxagen, Avidex, and Roche AG. He has had many speaking engagements funded by industry and the MRC and has served on numerous scientific advisory boards for universities and medical schools. He is on the board of Oxford Genetic Knowledge Park funded by the Department of Health.

Summary points

- Clinical research is in decline in the United Kingdom
- The main problems are in experimental medicine and clinical trials
- A national network for clinical research is needed to help coordinate funding and research programmes
- Better career and reward structures are needed for clinical researchers
- Funding must be increased from all sources

1 Doll R, Hill AB. Smoking and carcinoma of the lung. *BMJ* 1950;i:739-48.
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3 Chalmers I, Rounding C, Lock K. Descriptive survey of non-commercial randomised controlled trials in the United Kingdom, 1980-2002. *BMJ* 2003;327:1017-9.
4 Nuffield Trust for Research and Policy Studies. *Learning from experience: privacy and the secondary use of data in health research.* London: Nuffield Trust, 2002.

Corrections and clarifications

Understanding sensitivity and specificity with the right side of the brain

We introduced a typographical error when we redrew the summary figure for this article by Tze-Wey Loong, and unfortunately this was not noticed at the proof stage (27 September, pp 716-9). The bottom orange block should be labelled "Number of positive results" [not "Number of people with the disease"].

A history lesson

In this filler by Catriona Rundle (6 September, p 545) a bizarre editorial error that we have not yet been able to unravel led to the author's institution, Perth Royal Infirmary, being wrongly assigned to Perth in Western Australia (whose main hospital is Royal Perth Hospital) rather than to Perth in Scotland.